

Medical consequences of acute exposure to high altitude

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People who ascend rapidly to altitudes greater than 3,000 meters (10,000 ft) may become ill; rarely, some may die from an inability to adapt to hypoxia. Age, pre-existing cardiopulmonary or hematologic disease, and the rate and degree of ascent are known to limit man's adaptation to high altitudes. Other factors, such as blunted hypoxic respiratory drive and subclinical disease of the pulmonary vascular bed are probably also important. Pre-exposure with acetazolamide (Diamox) helps, but once symptoms of high altitude pulmonary edema (HAPE) occur, supplemental oxygen and rapid descent to lower altitudes are the only known remedies. In view of the steady increase in the number of people who work and play at high altitudes, physicians must understand the pathophysiologic mechanisms involved in order to treat properly and to counsel patients.

Exposure to altitudes over 3,000 meters rapidly or suddenly is known to cause many people discomfort, and it can subject a few to life-threatening disease. Although objective data are scarce because of logistical problems, many people complain of lassitude and headache; few will have frank pulmonary congestion and will collapse^{1,2}. Now that transportation to high altitudes has improved, and interest in work and play at high altitudes has increased, one may anticipate that more people will be at risk. Mountain-climbing and skiing are popular sports. They frequently take place at altitudes over 3,000 meters. Astronomers frequently work at 5,000 meters and above. Border conflicts resulting in military operations can involve thousands of people at high altitudes. Most of the illnesses and devastating consequences of high altitude exposure are avoidable.

Physiologic mechanisms

Although our knowledge of the mechanism is incomplete, hypoxia, of all of the physical factors involved, is the most important. As one ascends, barometric pressure and partial pressure of oxygen (PaO₂) fall, so that at 3,000 meters only 100 mm torr (torr = 1/760 of 1 atmosphere) of oxygen is available at one's mouth (Fig. 1). Even less is available to the cells of the body because of the oxygen cascade (Fig. 2), the

precise PaO₂ varies according to individual differences in ventilation, diffusion, and the ventilation-to-perfusion balance.

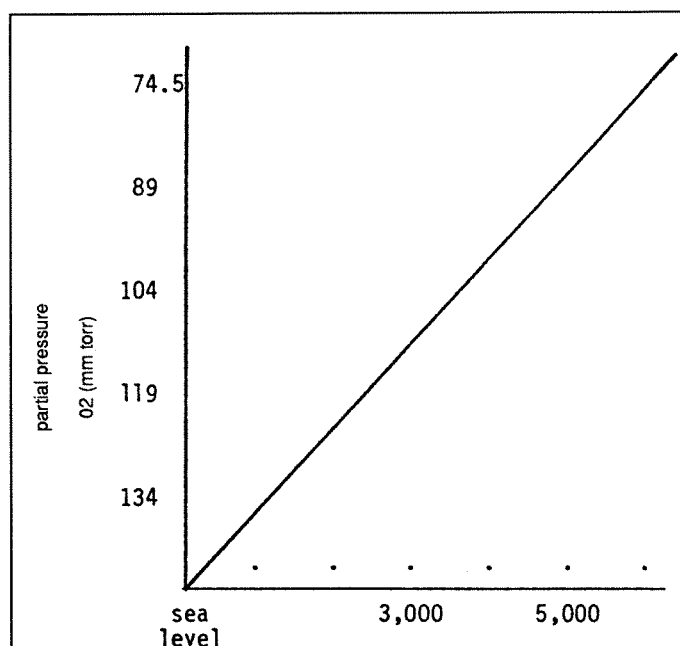


FIGURE 1: Relationship between altitude and concentration of inspired oxygen.

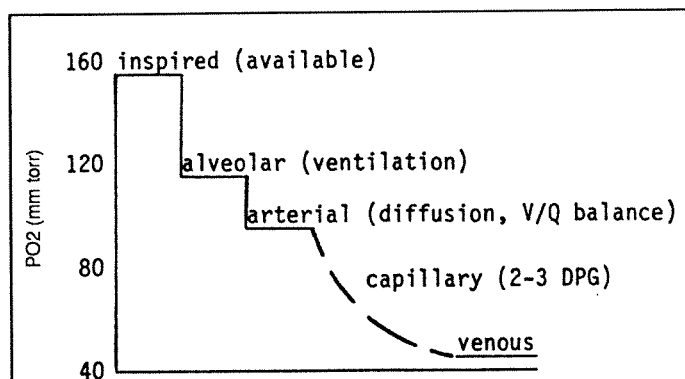
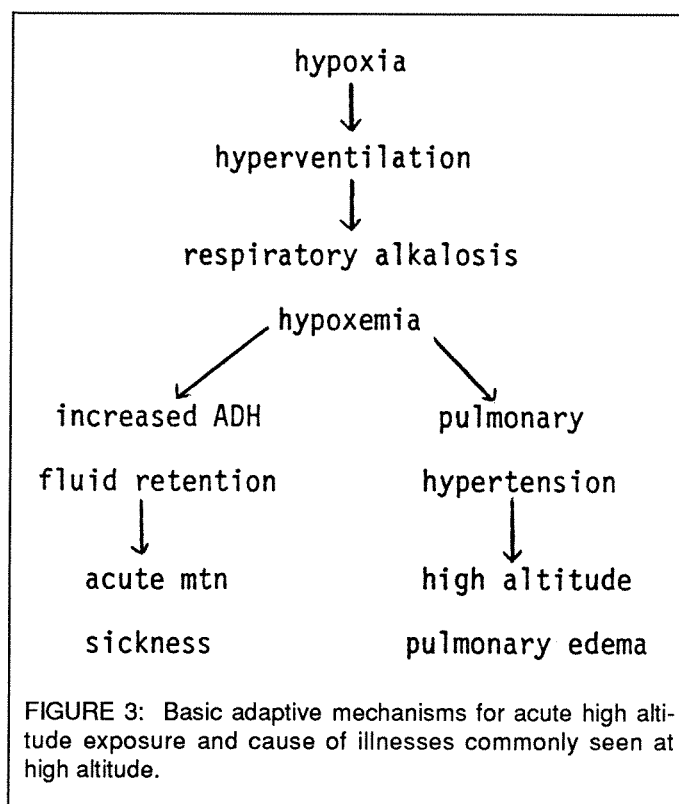


FIGURE 2: In the healthy subject, as one ascends (not shown) available oxygen is diminished and body tissues become more dependent on cardiopulmonary and hematologic mechanisms to supply adequate oxygen to tissues.

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Altitude (meters)	Disease (% incidence)	Common Symptoms	Treatment (* required)
2,000	hypoxemia (frequent)	dyspnea	slow ascent O ₂ prn
2-3,000	generalized (5) edema thrombophlebitis (rare)	swelling painful leg swelling	mild diuresis *descent for treatment
3-5,000	acute mtn (50) sickness high altitude pulm edema (1) retinal hemorrhage (1)	headache nausea fatigue dyspnea cough congestion blind spots	pretreatment Diamox ASA *O₂ *descent descent
5,000	cerebral (1) edema	severe headaches hallucinations neurologic deficits coma	*O₂ *descent steroids?

FIGURE 4: Life threatening illness rarely occurs in the healthy subject below 3,000 meters. *When such occurs, descent and supplemental oxygen are the only known treatments.

Since these measurements are not very commonly done at rest or during exercise one can expect and find a considerable variation in a person's adaptation to hypoxia. Besides this, hypoxia triggers a marked response by and in the body^{3,4} (Fig. 3).

The "hypoxic drive" causes hyperventilation (fortunately for most, the decreased density of air reduces the effort needed to respire). This does not completely obviate hypoxemia; it routinely causes respiratory alkalosis. Hypoxemia results in pulmonary artery vasoconstriction and hypertension. Alkalosis causes an increased production of 2,3-diphosphoglycerate (DPG). With an understanding of these basic facts, we are able to speculate on the mechanisms involved in the disorders usually seen at high altitude.

High altitude illnesses

As expected, symptoms and disease are related to the stress (precipitated by high altitude in relation to underlying conditions). In fact, serious illness does not occur at 2,000 meters. Everyone is affected at > 3,000 meters because of hypoxemia, but it is a failure in the adaptive mechanism, or the presence of an underlying medical condition, that may result in a serious disorder and, rarely, a life-threatening situation.

Diseases affecting "healthy" subject

1. Acute mountain illness. This is more uncomfortable than serious. Headache, nausea, weakness and shortness of breath are the usual symptoms which occur after rapid ascent to altitudes above 7,000 feet, and disappear after 1 to 2 days at that altitude. The suggested causative mechanism is hypoxemia with mild cerebral edema. This can be alleviated by prophylactic treatment with acetazolamide or by slow ascent.

2. High altitude cerebral edema and encephalopathy. In those who trek above 14,000 feet, a more severe dysfunction of the central nervous system occurs, though rarely, with hallucinations, sleepiness, symmetrical neurologic deficits and sometimes coma. Immediate descent, oxygen and perhaps steroids are indicated to prevent permanent neurologic deficits or death.

3. High altitude retinal hemorrhages. Small hemorrhages commonly occur and may temporarily affect vision, especially if they involve the macula. However, descent clears the hemorrhages and vision returns to normal.

4. High altitude pulmonary edema. The most common, severe, and potentially life-threatening disease that happens with moderate high altitude exposure is high altitude pulmonary edema (HAPE). HAPE affects young "healthy" subjects at above 3,000 meters and unless treated promptly and effectively may lead to death. The victim experiences chest pain, dyspnea and cough; this may rapidly lead to frank pulmonary edema. Supplemental oxygen must be given and the patient transported immediately to lower altitudes. The usual methods of treatment of pulmonary edema such as morphine, diuretics and digitalis are not efficacious and may complicate the picture by causing postural hypertension and shock. A slow ascent may be preventative, but premedication has no proven worth.

5. Generalized edema. Massive generalized edema may

(Continued) ►

occur in some people even at low altitudes and may respond to diuretics. Thrombophlebitis and pulmonary embolism are more likely to occur if treatment is not instituted promptly (Fig. 4).

In the healthy subject, diseases associated with high altitude exposure, though varied in expression, seem to have in common abnormal retention of water in tissues damaged by hypoxia, or because of inadequate "normal" mechanisms. To be on the safe side, oxygen should be given and descent advised. For the individual whose judgment seems to be clouded by hypoxia, this is always the prudent course. In a group that is experienced and has good judgment, symptomatic treatment for benign conditions is a satisfactory alternative.

High altitude exposure in patients with medical problems

In patients with diseases that are extremely sensitive to hypoxia, or whose adaptive mechanisms are poor, even moderate high-altitudes ($\leq 3,000$ meters) may cause problems.

1. Altered hypoxic response. In persons who do not adjust readily to hypoxia or who have blunted respiratory drives to alkalemia, high altitude may be dangerous. These are usually persons with disease-causing CO_2 retention even at sea level.

2. Patients in whom hypoxemia cannot be tolerated. Coronary artery disease, cerebral vascular insufficiency, sickle cell disease and severe anemia are obviously conditions that preclude exposure to high altitude.

3. Persons who cannot increase ventilation sufficiently. It seems paradoxical that many patients with chronic bronchitis and asthma do surprisingly well at high altitude. It is well-known that patients with obstructive lung disease may have obstruction in small or in large airways (or in some combination thereof). If obstruction is in the small airways, the decreased density of air at high altitudes offers no ease to the movement of air; these patients do badly. If obstruction is in the large airways, however, the rarefied air may actually be beneficial. No study has been reported (nor would it be entirely ethical) to test this hypothesis.

4. Restriction of the pulmonary capillary bed. HAPE occurs with alarming frequency in people with congenital absence of a main pulmonary artery⁶ and since the mechanism appears to be one of pre-capillary edema, these persons with mild to moderate loss of cross-sectional area of the capillary bed might be at greater risk. Patients with emphysema, pulmonary resection, or interstitial lung disease are at great risk and exposure to high altitudes should be discouraged. If HAPE can occur even in the "healthy", it is a given that patients with these disorders should be totally excluded.

The patient on cardiopulmonary medications likewise should also be discouraged from going to high altitudes because the effectiveness of these medications may be variable.

The use of drugs

Medications should be used sparingly and by those knowledgeable in the physiologic consequences and adaptations to high-altitude exposure.

1. Oxygen. Oxygen should always be available and used

freely if there is any doubt about what occurs. Lightweight, efficient, oxygen containers are available and easy to use.

2. Diuretics. Despite the relatively frequent symptoms and signs of excess fluid, these medications should be used with great care. The edema is usually extravascular so that a rapid diuresis may compound a difficult situation already begun. Acetazolamide is beneficial by preventing a blunted hypoxic drive and so should be used both *before* and *during* the ascent.

Other respiratory stimulants, such as progesterone, have some theoretical appeal but their side effects of fluid retention make them of lesser or of no value. A mild respiratory stimulant such as theophylline may be useful but, to my knowledge, it has not been properly evaluated.

3. Hypnotics and sedatives. Despite the frequent symptoms of muscle cramps, headache and sleeplessness, hypnotics and sedatives (including alcohol) because of their effect on respiratory drive and judgment should never be used.

4. Tobacco. Inadvertent inhalation of carbon monoxide ties up badly needed hemoglobin and should be strictly avoided (Fig. 5).

General advice to the person who plans to ascend rapidly includes the following:

- If you have known cardiopulmonary disease avoid exceeding 2,000 meters.
- If you are a healthy traveler who plans an ascent over 3,000 meters, you should take acetazolamide 250 mg tid the day before and the day of ascent.
- You should know the signs and symptoms of benign and significant high altitude illnesses and how to treat them.
- Oxygen and a planned route for rapid descent should always be available and taken if there is any suspicion of significant illness.
- The use of tobacco, alcohol, sedatives and hypnotics is strictly forbidden.
- If you plan to work at high altitudes, you should have a thorough medical evaluation that includes a history,

Drugs	Effect	Usefulness
O ₂	relieves hypoxemia	dyspnea, HAPE, cerebral edema
diuretics		
1) Diamox	causes acidosis increases hypoxic drive	pretreatment AMA
2) Lasix®	diuresis	generalized edema not HAPE
hypnotics, sedatives, alcohol	decreases drive impairs concentration	never
tobacco	binds Hgb	never

FIGURE 5: Pretreatment with Diamox and supplemental oxygen are the only medications proved useful at high altitude.

physical examination, complete blood count, chest roentgenogram and possibly exercise pulmonary function testing for hypoxic and hypercapnic drives.

g. Because of possible effects of hypoxemia on the fetus, if you are pregnant you should not ascend above 3,000 meters.

h. If you become ill at modest altitudes, a complete appraisal should be done at that point and further exposure to higher altitudes limited.

Conclusion

Rapid exposure to moderate (3,000 meters) and high (5,000 meters) altitudes is uncomfortable for most people and life-threatening for some. With a knowledge of the physiologic principles of adaptation to high altitude and understanding of the signs and symptoms of diseases associated with such

exposure, the physician and the traveler will be able to prevent both serious illness and death.

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OCCUPATIONAL HEALTH TRAINING (Continued from page 87)

State of Hawaii. In order to achieve these key health objectives, a large number of occupational-health professionals will be needed. The University of Hawaii School of Public Health expects to play an important role in their training.

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ENVIRONMENTAL EPIDEMIOLOGY (Continued from page 81)

dence of 1 in 1,000, a study population of 10,000 is required. The risk of having any cancer per year is 3-4 per 1,000 population. The incidence of having a particular cancer is much lower and the study group required must be much larger.

Other criteria for causality have to be considered, especially biologic plausibility. Toxicologic data from studies of cell cultures or in animals often supply information which cannot be duplicated in human studies because it is impossible to expose the latter to experimental doses of toxic agents. Caution is advised, therefore, when so-called plausibility is used as a substitute for detailed information.

What seems "reasonable" in regards to causality is not necessarily true. Even though environmental epidemiology has made very valuable contributions to our knowledge of environmental hazards, the results reported in every study should be critically evaluated, keeping in mind the difficulties inherent in their methodology.

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